Exhibit A

Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/863,823

4. An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP gene described in SEQ ID NO:6.

5. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:7; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:7.

7. A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. A host cell comprising the recombinant expression vector of claim 7.

9. (New) The isolated nucleic acid molecule of claim 4, comprising the nucleic acid sequence of SEQ ID NO:6.

10. (New) The recombinant expression vector of claim 7, wherein said nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:7.

11. (New) The recombinant expression vector of claim 10, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:6.

Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/691,343

4. An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP gene described in SEQ ID NO:6.

5. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:7; and

(b) hybridizes [under highly stringent conditions] to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:7.

7. A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. A host cell comprising the recombinant expression vector of claim 7.

9. (New) The isolated nucleic acid molecule of claim 4, comprising the nucleic acid sequence of SEQ ID NO:6.

10. (New) The recombinant expression vector of claim 7, wherein said nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:7.

11. (New) The recombinant expression vector of claim 10, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:6.

1: Nat Cell Biol 2000 May;2(5):302-9

Related Articles, Link

nature cell biology

PDGF-C is a new protease-activated ligand for the PDGF alpha-receptor.

Li X, Ponten A, Aase K, Karlsson L, Abramsson A, Uutela M, Backstrom G, Hellstrom M, Bostrom H, Li H, Soriano P, Betsholtz C, Heldin CH, Alitalo K, Ostman A, Eriksson U.

Ludwig Institute for Cancer Research, Stockholm, Sweden.

Platelet-derived growth factors (PDGFs) are important in many types of mesenchymal cell. Here we identify a new PDGF, PDGF-C, which binds to and activates the PDGF alpha-receptor. PDGF-C is activated by proteolysis and induces proliferation of fibroblasts when overexpressed in transgenic mice. In situ hybridization analysis in the murine embryonic kidney shows preferential expression of PDGF-C messenger RNA in the metanephric mesenchyme during epithelial conversion. Analysis of kidneys lacking the PDGF alpha-receptor shows selective loss of mesenchymal cells adjacent to sites of expression of PDGF-C mRNA; this is not found in kidneys from animals lacking PDGF-A or both PDGF-A and PDGF-B, indicating that PDGF-C may have a unique function.

PMID: 10806482 [PubMed - indexed for MEDLINE]

1: J Biol Chem 2001 Jul 20;276(29):27406-14 Related Articles, Link

Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor.

Gilbertson DG, Duff ME, West JW, Kelly JD, Sheppard PO, Hofstrand PD, Gao Z, Shoemaker K, Bukowski TR, Moore M, Feldhaus AL, Humes JM, Palmer TE, Hart CE.

ZymoGenetics Inc., Seattle, Washington 98102, USA. gilbertd@zgi.com

We have characterized platelet-derived growth factor (PDGF) C, a novel growth factor belonging to the PDGF family. PDGF-C is a multidomain protein with the N-terminal region homologous to the extracellular CUB domain of neuropilin-1, and the C-terminal region consists of a growth factor domain (GFD) with homology to vascular endothelial growth factor (25%) and PDGF A-chain (23%). A serum-sensitive cleavage site between the two domains allows release of the GFD from the CUB domain. Competition binding and immunoprecipitation studies on cells bearing both PDGF alpha and beta receptors reveal a high affinity binding of recombinant GFD (PDGF-CC) to PDGF receptor-alpha homodimers and PDGF receptor-alpha/beta heterodimers. PDGF-CC exhibits greater mitogenic potency than PDGF-AA and comparable or greater mitogenic activity than PDGF-AB and PDGF-BB on several mesenchymal cell types. Analysis of PDGF-CC in vivo in a diabetic mouse model of delayed wound healing showed that PDGF-CC significantly enhanced repair of a full-thickness skin excision. Together, these studies describe a third member of the PDGF family (PDGF-C) as a potent mitogen for cells of mesenchymal origin in in vitro and in vivo systems with a binding pattern similar to PDGF-AB.

PMID: 11297552 [PubMed - indexed for MEDLINE]

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☐ **1:** NM_016205. Homo sapiens plat...[gi:9994186] Links

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  AUTHORS   Li,X., Ponten,A., Aase,K., Karlsson,L., Abramsson,A., Uutela,M.,
            Backstrom,G., Hellstrom,M., Bostrom,H., Li,H., Soriano,P.,
            Betsholtz,C., Heldin,C.H., Alitalo,K., Ostman,A. and Eriksson,U.
  TITLE     PDGF-C is a new protease-activated ligand for the PDGF
            alpha-receptor
  JOURNAL   Nat. Cell Biol. 2 (5), 302-309 (2000)
  MEDLINE   20268201
   PUBMED   10806482
REFERENCE   2  (bases 1 to 3007)
  AUTHORS   Hamada,T., Ui-Tei,K. and Miyata,Y.
  TITLE     A novel gene derived from developing spinal cords, SCDGF, is a
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  JOURNAL   FEBS Lett. 475 (2), 97-102 (2000)
  MEDLINE   20317014
   PUBMED   10858496
REFERENCE   3  (bases 1 to 3007)
  AUTHORS   Tsai,Y.J., Lee,R.K., Lin,S.P. and Chen,Y.H.
  TITLE     Identification of a novel platelet-derived growth factor-like gene,
            fallotein, in the human reproductive tract
  JOURNAL   Biochim. Biophys. Acta 1492 (1), 196-202 (2000)
  MEDLINE   20461776
   PUBMED   11004490
REFERENCE   4  (bases 1 to 3007)
  AUTHORS   Zwerner,J.P. and May,W.A.
  TITLE     PDGF-C is an EWS/FLI induced transforming growth factor in Ewing
            family tumors
  JOURNAL   Oncogene 20 (5), 626-633 (2001)
  MEDLINE   21214457
   PUBMED   11313995
REFERENCE   5  (bases 1 to 3007)
  AUTHORS   Uutela,M., Lauren,J., Bergsten,E., Li,X., Horelli-Kuitunen,N.,
            Eriksson,U. and Alitalo,K.
  TITLE     Chromosomal location, exon structure, and vascular expression
            patterns of the human PDGFC and PDGFC genes
  JOURNAL   Circulation 103 (18), 2242-2247 (2001)
  MEDLINE   21266739
   PUBMED   11342471
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REFERENCE 6 (bases 1 to 3007)
AUTHORS Gilbertson,D.G., Duff,M.E., West,J.W., Kelly,J.D., Sheppard,P.O., Hofstrand,P.D., Gao,Z., Shoemaker,K., Bukowski,T.R., Moore,M., Feldhaus,A.L., Humes,J.M., Palmer,T.E. and Hart,C.E.
TITLE Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor
JOURNAL J. Biol. Chem. 276 (29), 27406-27414 (2001)
MEDLINE 21347863
PUBMED 11297552
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Summary: The protein encoded by this gene is a member of the platelet-derived growth factor family. The four members of this family are mitogenic factors for cells of mesenchymal origin and are characterized by a core motif of eight cysteines. This gene product appears to form only homodimers. It differs from the platelet-derived growth factor alpha and beta polypeptides in having an unusual N-terminal domain, the CUB domain.
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Revised: July 5, 2002.

Mar 3 2003 10:13:39

1: AF260738. Homo sapiens plat...[gi:14009503]

Links

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  AUTHORS   Gilbertson,D.G., Duff,M.E., West,J.W., Kelly,J.D., Sheppard,P.O.,
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            Feldhaus,A.L., Humes,J.M., Palmer,T.E. and Hart,C.E.
  TITLE     Platelet-derived growth factor C (PDGF-C), a novel growth factor
            that binds to PDGF alpha and beta receptor
  JOURNAL   J. Biol. Chem. 276 (29), 27406-27414 (2001)
  MEDLINE   21347863
   PUBMED   11297552
REFERENCE   2  (bases 1 to 1804)
  AUTHORS   Gao,Z., Hart,C., Piddington,C., Sheppard,P., Shoemaker,K.,
            Gilbertson,D., West,J. and O'Hara,P.J.
  TITLE     Direct Submission
  JOURNAL   Submitted (26-APR-2000) Biomolecular Informatics, ZymoGenetics,
            Inc., 1201 Eastlake Avenue East, Seattle, WA 98102, USA
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Revised: July 5, 2002.

Mar 3 2003 10:13:39

☐ 1: Biochim Biophys Acta 2000 Jun 21;1492(1):196-202 Related Articles, Link

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract.

Tsai YJ, Lee RK, Lin SP, Chen YH.

Division of Reproduction and Endocrinolgy, Department of Medical Research, Mackay Memorial Hospital, Tamshui, Taiwan.
yjtsai@ms1.mmh.org.tw

We isolated the cDNA of a novel platelet-derived growth factor-like gene from human endometrium. The gene was named fallotein; it was 3007 bases in length, and encoded a protein of 345 amino acids. Antiserum against the fallotein protein can recognize a specific protein in the fallopian tube, with a molecular size in accordance with the anticipated size of fallotein. Fallotein mRNA is expressed in two molecular sizes, 3.8 and 2.9 kb, with the former being more abundant. High expression of the gene was found in the prostate, testis, and uterus. A weaker expression signal was found in the spleen, thymus, and small intestine, but expression of fallotein in the colon and peripheral blood leukocytes was negligible.

PMID: 11004490 [PubMed - indexed for MEDLINE]

>AF091434 ACCESSION:AF091434 NID: gi 6002592 gb AF091434.1 AF091434
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fallotein mRNA, complete cds
Length = 3007

Score = 486 bits (1237), Expect = e-135
Identities = 234/234 (100%), Positives = 234/234 (100%)
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☐ **1:** AF091434. Homo sapiens secr...[gi:6002592] Links

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VERSION     AF091434.1  GI:6002592
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REFERENCE   1  (bases 1 to 3007)
  AUTHORS   Tsai,Y.J., Lee,R.K., Lin,S.P. and Chen,Y.H.
  TITLE     Identification of a novel platelet-derived growth factor-like gene,
            fallotein, in the human reproductive tract
  JOURNAL   Biochim. Biophys. Acta 1492 (1), 196-202 (2000)
  MEDLINE   20461776
   PUBMED   11004490
REFERENCE   2  (bases 1 to 3007)
  AUTHORS   Tsai,Y.J., Lee,R.K.K. and Lin,S.P.
  TITLE     Direct Submission
  JOURNAL   Submitted (14-SEP-1998) Dept. Medical Research, Mackay Memorial
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Revised: July 5, 2002.

1: FEBS Lett 2000 Jun 16;475(2):97-102 Related Articles, Link

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/VEGF family.

Hamada T, Ui-Tei K, Miyata Y.

Department of Pharmacology, Nippon Medical School, Tokyo, Japan.

We isolated a novel gene designated spinal cord-derived growth factor (SCDGF). Its expression was increased in chick spinal cords with embryonic development and decreased after hatching. The amino acid sequences of chick and human SCDGFs revealed a putative signal sequence followed by a CUB domain and a region homologous to the members of the platelet-derived growth factor/vascular endothelial growth factor family. Furthermore, human SCDGF secreted from the cells showed a mitogenic activity for 10T1/2 cells in vitro. These results led us to speculate that SCDGF plays an important role in the development of the spinal cord.

PMID: 10858496 [PubMed - indexed for MEDLINE]

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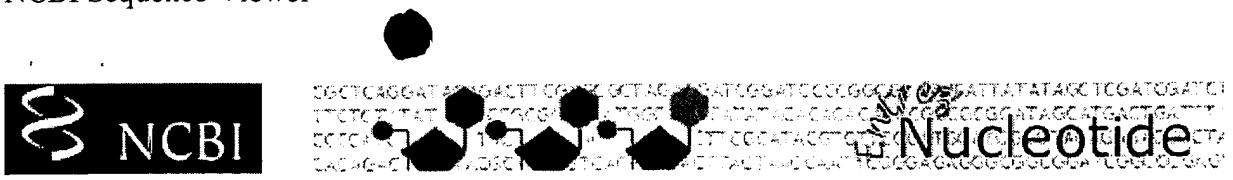

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REFERENCE   1  (sites)
  AUTHORS   Hamada,T., Ui-Tei,K. and Miyata,Y.
  TITLE     A novel gene derived from developing spinal cords, SCDGF, is a
            unique member of the PDGF/VEGF family
  JOURNAL   FEBS Lett. 475 (2), 97-102 (2000)
  MEDLINE   20317014
   PUBMED   10858496
REFERENCE   2  (bases 1 to 1817)
  AUTHORS   Hamada,T., Ui-Tei,K. and Miyata,Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-OCT-1999) Tsuyoshi Hamada, Nippon Medical School,
            Department of Pharmacology; 1-1-5, Sendagi, Bunkyo-ku, Tokyo
            113-8602, Japan (E-mail:t-hamada@nms.ac.jp,
            Tel:81-3-3822-2131(ex.5277), Fax:81-3-5814-1684)
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Revised: July 5, 2002.

Mar 3 2003 10:13:39

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             |||||||||||||||||||||||||||||||||||||
Sbjct: 74725 aatgtttcaagaatgtatgacatatgacttaacttaa 74689


 Score =  414 bits (209), Expect = e-113
 Identities = 209/209 (100%)
 Strand = Plus / Minus


Query: 496   caattcacagaagctgtgagtccttcagtgctaccccttcagctttgccactggacctg 555
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 77153 caattcacagaagctgtgagtccttcagtgctaccccttcagctttgccactggacctg 77094


Query: 556   cttaataatgctataactgcctttagtaccttggaagaccttattcgatatcttgaacca 615
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 77093 cttaataatgctataactgcctttagtaccttggaagaccttattcgatatcttgaacca 77034


Query: 616   gagagatggcagttggacttagaagatctatataggccaacttggcaacttcttggcaag 675
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 77033 gagagatggcagttggacttagaagatctatataggccaacttggcaacttcttggcaag 76974
```

```
Query: 676   gcttttgtttttggaagaaaatccagagg 704
              ||||||||||||||||||||||||||||
Sbjct: 76973 gcttttgtttttggaagaaaatccagagg 76945


 Score =  396 bits (200), Expect = e-108
 Identities = 200/200 (100%)
 Strand = Plus / Minus


Query: 118    ggagtacaagatcctcagcatgagagaattattactgtgtctactaatggaagtattcac 177
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 154677 ggagtacaagatcctcagcatgagagaattattactgtgtctactaatggaagtattcac 154618


Query: 178    agcccaaggtttcctcatacttatccaagaaatacggtcttggtatggagattagtagca 237
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 154617 agcccaaggtttcctcatacttatccaagaaatacggtcttggtatggagattagtagca 154558


Query: 238    gtagaggaaaatgtatggatacaacttacgtttgatgaaagatttgggcttgaagaccca 297
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 154557 gtagaggaaaatgtatggatacaacttacgtttgatgaaagatttgggcttgaagaccca 154498


Query: 298    gaagatgacatatgcaagta 317
              ||||||||||||||||||||
Sbjct: 154497 gaagatgacatatgcaagta 154478


 Score =  361 bits (182), Expect = 5e-97
 Identities = 185/186 (99%)
 Strand = Plus / Minus


Query: 310    tgcaagtatgattttgtagaagttgaggaacccagtgatggaactatattagggcgctgg 369
              |||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 115282 tgcaggtatgattttgtagaagttgaggaacccagtgatggaactatattagggcgctgg 115223


Query: 370    tgtggttctggtactgtaccaggaaaacagatttctaaaggaaatcaaattaggataaga 429
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 115222 tgtggttctggtactgtaccaggaaaacagatttctaaaggaaatcaaattaggataaga 115163


Query: 430    tttgtatctgatgaatattttccttctgaaccagggttctgcatccactacaacattgtc 489
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 115162 tttgtatctgatgaatattttccttctgaaccagggttctgcatccactacaacattgtc 115103


Query: 490    atgcca 495
              ||||||
Sbjct: 115102 atgcca 115097
```

>AC093325.3.1.130754
Length = 130754

Score = 236 bits (119), Expect = 2e-59
Identities = 119/119 (100%)
Strand = Plus / Minus

```
Query: 1     atgagcctcttcgggcttctcctgctgacatctgccctggccggccagagacaggggact 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 80211 atgagcctcttcgggcttctcctgctgacatctgccctggccggccagagacaggggact 80152


Query: 61    caggcggaatccaacctgagtagtaaattccagttttccagcaacaaggaacagaacgg 119
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 80151 caggcggaatccaacctgagtagtaaattccagttttccagcaacaaggaacagaacgg 80093
```

☐ **1:** AC092608. Homo sapiens BAC ...[gi:15668121] Links

```
LOCUS       AC092608              196952 bp    DNA     linear   PRI 01-MAR-2002
DEFINITION  Homo sapiens BAC clone RP11-154F14 from 4, complete sequence.
ACCESSION   AC092608 AC009582
VERSION     AC092608.2  GI:15668121
KEYWORDS    HTG.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 196952)
  AUTHORS   Sulston,J.E. and Waterston,R.
  TITLE     Toward a complete human genome sequence
  JOURNAL   Genome Res. 8 (11), 1097-1108 (1998)
  MEDLINE   99063792
   PUBMED   9847074
REFERENCE   2  (bases 1 to 196952)
  AUTHORS   Isak,A., Kozlowicz,A. and Hawkins,M.
  TITLE     The sequence of Homo sapiens BAC clone RP11-154F14
  JOURNAL   Unpublished (2001)
REFERENCE   3  (bases 1 to 196952)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (19-JUL-2001) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
REFERENCE   4  (bases 1 to 196952)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (19-SEP-2001) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
REFERENCE   5  (bases 1 to 196952)
  AUTHORS   Waterston,R.
  TITLE     Direct Submission
  JOURNAL   Submitted (01-MAR-2002) Department of Genetics, Washington
            University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA
COMMENT     On Sep 19, 2001 this sequence version replaced gi:14916193.
            -------------- Genome Center
                Center: Washington University Genome Sequencing Center
                Center code: WUGSC
                Web site: http://genome.wustl.edu/gsc
                Contact: sapiens@watson.wustl.edu
            -------------- Summary Statistics
                Center project name: H_NH0154F14
                Drafting Center: WIBR
            --------------.
```

☐ **1:** AC093325. Homo sapiens BAC ...[gi:15982602] Links

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LOCUS       AC093325              130754 bp    DNA     linear   PRI 09-JAN-2002
DEFINITION  Homo sapiens BAC clone RP11-612J15 from 4, complete sequence.
ACCESSION   AC093325
VERSION     AC093325.3  GI:15982602
KEYWORDS    HTG.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 130754)
  AUTHORS   Sulston,J.E. and Waterston,R.
  TITLE     Toward a complete human genome sequence
  JOURNAL   Genome Res. 8 (11), 1097-1108 (1998)
  MEDLINE   99063792
   PUBMED   9847074
REFERENCE   2  (bases 1 to 130754)
  AUTHORS   Waligorski,J. and Haakenson,W.
  TITLE     The sequence of Homo sapiens BAC clone RP11-612J15
  JOURNAL   Unpublished (2002)
REFERENCE   3  (bases 1 to 130754)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (18-AUG-2001) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
REFERENCE   4  (bases 1 to 130754)
  AUTHORS   Waterston,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (07-OCT-2001) Genome Sequencing Center, Washington
            University School of Medicine, 4444 Forest Park Parkway, St. Louis,
            MO 63108, USA
REFERENCE   5  (bases 1 to 130754)
  AUTHORS   Waterston,R.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-JAN-2002) Department of Genetics, Washington
            University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA
COMMENT     On Oct 7, 2001 this sequence version replaced gi:15624997.
            -------------- Genome Center
                Center: Washington University Genome Sequencing Center
                Center code: WUGSC
                Web site: http://genome.wustl.edu/gsc
                Contact: sapiens@watson.wustl.edu
            -------------- Summary Statistics
                Center project name: H_NH0612J15
            --------------.

            NOTICE:  This sequence may not represent the entire insert of this
```